UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/981,648 | 10/16/2001 | Frank L. Graham | ADVEC10IA-C2 | 8065 |

29847 7590 09/11/2002

VAN DYKE & ASSOCIATES, P.A.
1630 HILLCREST STREET
ORLANDO, FL 32803

| EXAMINER |
|---|
| KATCHEVES, KONSTANTINA T |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1636 | |

DATE MAILED: 09/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/981,648 | GRAHAM ET AL. | |
| | Examiner | Art Unit | |
| | Konstantina Katcheves | 1636 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-23 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-23 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

## DETAILED ACTION

Claims 1-23 are pending in the present application.

### *Election/Restrictions*

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-18, 22 and 23, drawn to a method for making an infectious agent, a recombinant adenovirus vector system and kit, classified in class 435, subclass 320.1.

II. Claim 19, drawn to a modified cell, classified in class 435, subclass 325.

III. Claims 20 and 21, drawn to a method for vaccinating, classified in class 424, subclass 1.17.

IV. Claims 20-21, drawn to a method for gene therapy, classified in class 514, subclass 44.

The inventions are distinct, each from the other because of the following reasons:

Inventions I, II, III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions each comprise either a different product or different method wherein each is separately patentable from each of the others. For instance, Groups I, III and IV relate to different methods each having different and unique method steps and different considerations

such that a search for one would not necessarily be coextensive with a search for another. Thus, the search of these methods together would present an undue search burden to the examiner. Moreover, the cell of Group III is a completely different product than the product recited in Group I. Although an adenovirus may infect a cell, cells have different physiological and structural characteristics than the adenovirus of Group I rendering them different products.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Moreover, the search required for each of the above groups is not required for the other such that restriction is proper.

During a telephone conversation with Joe Fischer on 27 August 2002, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-18, 22 and 23. Affirmation of this election must be made by applicant in replying to this Office action. Claims 21 and 22 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,379,943. Although the conflicting claims are not identical, they are not patentably distinct from each other because contain limitations which overlap, or the claims recite overlapping groups of plasmids, or other specific nucleic acid sequences. Further, the plasmids or nucleic acid sequences are used for the same purpose: construction of infectious adenovirus vectors. The claims of the prior US patent recite a method for making an infectious adenovirus which comprises a first nucleic acid sequence encoding adenovirus sequences which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus and a second nucleic acid sequence which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus. The present claims differ in that they require head to head ITR junctions. Although not specifically claimed in the prior US patent the claims of the prior patent embrace the instant claims because they provide for the efficient and reliable

isolation of viral vectors using recombinase pathways. The methods of the prior patent would embrace the instant claims because the plasmids used in the prior patent do contain head to head ITRs such that the instant claims are an obvious variation on the prior claims.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, 11, 13, 17, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaleko (WO 97/25446).

The invention of the instant claims is drawn to a method of generating adenoviral vectors infectious adenovirus which comprises a first nucleic acid sequence encoding adenovirus sequences which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus and a second nucleic acid sequence which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus. Each of the vectors in the present invention comprise a head to head inverted terminal repeat (ITR).

Kaleko teaches a method for generating adenoviral vectors using recombinase-mediated transfer. See pages 5-9. The method uses a first polynucleotide including a heterologous DNA to be expressed, one adenoviral inverted terminal repeat (ITR), an adenoviral packaging signal and a recombinase target site. The second polynucleotide includes an adenoviral ITR. The second

polynucleotide can also be a helper virus in which the adenoviral terminal protein is attached to the ITR. See page 12. As shown in, Figures 7, 10, 19, and 24, the helper virus can contain two ITRs. Although the DL327lox sequence in the figures is shown as linear, it is interpreted that the ITRs are in a head-to-head orientation. If the sequence had been depicted as a circle, it is presumably drawn in a linear fashion because the terminal proteins are attached. See also pages 26-27. Adenoviral proteins for replication and packaging can be on the first polynucleotide, the second polynucleotide, a third polynucleotide provided by the cell, or any combination thereof. The packaging signal can be deleted from the adenoviral sequences. See pages 12-13.

Claims 1, 2, 6, 8, 11, 13, 15, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Bett *et al.* (1994, Proc. Natl. Acad. Sci. USA 91:8802-6).

The invention of the instant claims is drawn to a method of generating adenoviral vectors infectious adenovirus which comprises a first nucleic acid sequence encoding adenovirus sequences which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus and a second nucleic acid sequence which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus. Each of the vectors in the present invention comprise a head to head inverted terminal repeat (ITR). The invention of the instant claims also recites a deletion in the E1 region of the adenoviral vector.

Bett *et al.* (1994) teach construction of an infectious adenovirus vector by the recombination of two sequences. As shown in Figure 3, one of the sequences, a pBGH plasmid, contains a head-to-head ITR junction indicated by the two arrows at the top of the plasmid.

There is sufficient overlapping sequence for homologous recombination between the sequences when cotransfected into a cell such that the limitation of the present claims requiring sufficient overlap in the sequences for the purposes of recombination is met. The cells used are 293 cells and as such, they express E1 function. See notes on 293 cells in the instant specification on page 2, lines 4-5. See Fig. 3 of Bett et al.

Claims 1, 2, 3, 6, 8, 11, 13, 15, 22 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Bett *et al.* (1993, J. Virology 67:5911-21).

The invention of the instant claims is drawn to a method of generating adenoviral vectors infectious adenovirus which comprises a first nucleic acid sequence encoding adenovirus sequences which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus and a second nucleic acid sequence which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus. Each of the vectors in the present invention comprise a head to head inverted terminal repeat (ITR). The invention of the instant claims also recites a deletion in the E1 region of the adenoviral vector.

Bett *et al.* (1993) teach the construction of infectious adenovirus vectors by recombination between two nucleic acid sequences. In Figure 3 of the reference, a recombination between plasmid pFG173 and a pAB plasmid produces the infectious virus. Both pFG173 and the pAB plasmid contain head-to-head ITR junctions, as interpreted from the "100/0 mu" notation above each plasmid, which represents locations on the adenovirus vector where the ITRs reside. Additionally, figure 9b of the instant specification teaches a pAB vector that contains a foreign DNA insert and pFG173, and both are drawn with the two arrows at the top of

the plasmid designating the head-to-head ITR junction. In the reference, the pAB vector is shown as having a deletion in E1 (see the topmost plasmid in the figure). The plasmids are cotransfected into 293 cells, which express E1 (see above rejection over Bett, 1994).

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-19, 22 and 23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Claim 3 is drawn to a method wherein a plasmid includes a "deletion or modification in E1 that renders the adenoviral sequences insufficient to form infections, viruses and combinations thereof." Claim 4, 16, 17, and 18 recite adenovirus DNA having a deletion or mutation of a gene. Claim 5 recites a modification in an E1 sequence extending beyond the packaging signal of claim 4, adenoviral E3 gene, adenoviral E4 and combinations thereof. Claim 18 also recites various genes or "combinations thereof." Claims 7, 9, 12, 14, 19, and 21 recite various plasmids and identifiable combinations thereof. Claim 11 recites a "portion of" viral DNA.

Applicant has failed to describe the sequences of the above claims in such full clear and concise terms such that one of skill in the art would reasonably conclude that applicant was in possession of the invention claimed. Applicant claims partial sequences, mutations, deletions, combinations of sequences and combinations of plasmids yet does not disclose what these mutations, deletions or portions of sequences are. These are genus claims that encompass a wide array of molecules. The specification does not disclose the multitude of partial sequences, mutations, deletions, and combinations of sequences or combinations of plasmids that these claims embrace. Moreover, the specification fails to provide teachings how the structures of these molecules relate to their function. Thus, the specification does not describe the complete structure of a representative number of species. Neither does the specification describe a representative number of species in terms of partial structure and relevant identifying characteristics.

Claims 7, 9, 12 and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the plasmids of these claims are required to practice the claimed inventions. Thus, these must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the plasmids. Although the Applicants describe the construction of the plasmids in the Figures, it is not clear that all of the nucleic acid sequences from which the plasmids were constructed are readily available to the public, and thus the plasmids of the claims may not be obtainable without deposit.

Where the invention involves a biological material and words alone cannot sufficiently describe how to make and use the invention in a reproducible manner, access to the biological material may be necessary for the satisfaction of the statutory requirements for patentability under 35 U.S.C. 112. Courts have recognized the necessity and desirability of permitting an applicant for a patent to supplement the written disclosure in an application with a deposit of biological material which is essential to meet some requirement of the statute with respect to the claimed invention. Merck and Co., Inc. v. Chase Chemical Co., 273 F. Supp. 68, 155 USPQ 139 (D. N.J. 1967); In re Argoudelis, 434 F.2d 666, 168 USPQ 99 (CCPA 1970).

Applicant claims various plasmid constructs in the instant claims. In order to sufficiently enable the claimed plasmids, Applicant must make a biological deposit of each of them. The

deposit rules pursuant to 37 CFR 1.801 - 1.809 set forth examining procedures and conditions of deposit which must be satisfied when a deposit is required. See MPEP 2402-2404.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-23 recite the terms "insufficient" and "sufficient." These terms are relative in nature, which render the claims indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 11 is are vague and indefinite as to the metes and bounds of the claim because they claim an expression cassette "derived from" a plasmid and a viral DNA "derived from" a plasmid. "Derived" is a term that is non-specific and relative in nature for which Applicant provides no definition. It provides no clarity as to what Applicant's claimed invention includes and what it does not include. Without a more specific definition of the claim, it is impossible to determine what and how many derivations comprise the invention. The nature and number of the derivations to arrive at the invention Applicant seeks to protect with the patent are not established such that a person skilled in the art would be apprised of the metes and bounds of the claims. The limits of the inventions cannot be discerned and others could not possibly know if they were infringing Applicant's claim.

Claim 5 recites an adjective that appears to be inappropriate. The word "of" in line 2 of the claim appears to be grammatically unnecessary.

Claim 5 also recite the language "extending beyond said packaging signal." This language renders the claim vague because it raises several questions including: how far beyond the packaging signal is the sequence, how many nucleotides in length is this sequence contemplated and in what direction beyond the packaging signal is this sequence.

Claims 14, 19 and 21 recite the language, "as optionally needed" which renders the present claims vague and indefinite to one of skill in the art. This terminology raises a question as to whether applicant intends the phrase immediately following "as optionally needed" to be a limitation. Because of this ambiguity one of skill in the art would not be apprised of the metes and bounds of the claims.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (703) 305-1999. The examiner can normally be reached on Monday through Friday 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3388.

Konstantina Katcheves
August 29, 2002

JAMES KETTER
PRIMARY EXAMINER